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Nitrobenzene Poisoning (A Case Report) Methhemoglobinemia Due to Nitrobenzene Ingestion (Paint Solvent, Oil of Mirbane)

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ABSTRACT : *A case of acute poisoning with nitrobenzene is presented where clinical evaluation and timely management, with repeated intravenous methylene blue & Blood transfusions helped to save a life. It is important to take care of the secondary cycling of nitrobenzene from body stores in patients presenting late, after heavy exposure.*

KEYWORDS: *Acute methaemoglobinaemia, methylene blue, nitrobenzene poisoning*

I. INTRODUCTION

Acute poisoning with nitrobenzene causing significant methaemoglobinaemia is uncommon but life threatening emergency. Early aggressive management of severe poisoning, strongly suspected on clinical grounds may change the outcome of a patient.

II. CASE REPORT

A 30-year-old,irritable,anxious male presented to emergency referred from other center on mechanical ventillation with cyanosis and a greyish-brown hue, laboured respiration of 26/min, BP 129/74 mm of Hg, pulse rate 74/min, pupils with sluggish reaction, and SpO_2 of 89% only. There was a history of severe pain in the abdomen, nausea, vomiting, and dizziness, which was treated on admission at primary center.There at primary center oral methylene blue was given(5 ml.12 hrly),as to non-availability of IV.An urgent ultrasound abdomen ruled out any abdominal catastrophe and showed a generalized mild-to-moderate hepatic inflammation. Blood samples drawn for ABG had a chocolate brown colour, which did not improve on exposure to 100% oxygen and showed compensated metabolic acidosis ; X-ray of the chest and ECG were within normal limits, and WBC and liver enzymes were markedly raised. Serum creatinine and blood urea were within normal range. Hemoglobin at admission was 9.4gm%,which dropped down to 6.3gm% on 9^{th} day. Similarly S.bilirubin at admission was 2.0mg% which was raised to 13.0 mg%. A clinical diagnosis of severe acute methaemoglobinaemia of nitrobenzene poisoning was made.

100mg of methylene blue (prepared as 1% sterile solution), repeated after 12 hrs., were given IV. This improved his SpO_2 to 92%, Intravenous vitamin K; vitamin C, 10% dextrose, anxiolytics, oral iron, and an antibiotic IV were also added. Urine output was maintained above 100 ml/hour with proper hydration, maintaining a normal central venous pressure (CVP).Multiple blood & blood products(FFP),were transfused. Patient at admission had severe hypokalemia(2.5mEq/L),which was corrected by IV slow potassium infusion. Meth-hemoglobin estimation in blood was done & it was significantly high (11.1 units as compared to normal values of 0.00 to 2.0.) He was extubated at 48 hours and maintained on a *continuous positive airway pressure* (CPAP) mask, with ABG showing a saturation of 93% and a PaO_2 of 112. He improved rapidly after the 10th day with an $SpO_2$of 90% on room air. Patient had a single episode of GTCS on day 11^{th} & was epsolinised followed by oral dilantin tablets (100mg TDS).CT head was absolutely normal. Although the liver enzymes were raised. He was discharged on the 14th day on oral iron, folate , ascorbic acid, and liver enzyme supplements and breathing exercises.

III. DISCUSSION

Nitrobenzene, a pale yellow oily liquid, with an odour of bitter almonds is used as an intermediate in the synthesis of solvents, like paint remover. The first report of nitrobenzene poisoning came in 1886[1] and subsequent fatality reports followed[1,2]. Intoxication can be accidental or suicidal. Accidental toxicity can occur in patients consuming well water with dangerously high levels of nitrites and nitrates[3]. The lethal dose is reported to range from 1 g to 10 g, by different authors[4,5]. A review of published reports does not provide any consistent

reports regarding fatalities and dose of ingestion[5].The toxic effects after ingestion are due to the rapid development of methaemoglobinaemia[4], a condition in which the iron within the haemoglobin is oxidized from the ferrous (Fe^{2+}) state to the ferric (Fe^{3+}) state, resulting in the inability to transport oxygen and causes a brownish discolouration of the blood[3]. Once formed, methemoglobin can be reduced enzymatically either via an Adenine dinucleotide (NADH)-dependent reaction, catalysed by cytochrome b5 reductase, or an alternative pathway utilizing the nicotine adenine dinucleotide phosphate.

Cyanosis(at 20%), headache, dyspnea, chest pain, tachypnea, and tachycardia develop. At 40 – 50%, confusion, lethargy, and metabolic acidosis occur leading to coma, seizures, bradycardia, ventricular dysrythmia, and hypertension. Fractions around 70% are fatal. Anemic or G6PD-deficient patients suffer more severe symptoms[2,4]. Leukocytosis has been reported, with relative lymphopenia[5].
Other effects include hepatosplenomegaly, altered liver functions, and Heinz body haemolytic anaemia[2,6]. Nitrobenzene is metabolized to p-nitrophenol and aminophenol and excreted in urine, up to 65%, and in stools up to 15%, after five days of ingestion. Liver stomach, blood, and brain may act as stores and release it gradually[6].
Clues for diagnosis include a history of chemical ingestion, the characteristic smell of bitter almonds, persisting cyanosis on oxygen therapy without severe cardiopulmonary disease, low arterial oxygen saturation, with normal ABG (calculated) oxygen saturation. Dark brown blood that fails to turn bright red on shaking, which suggests methaemoglobinaemia and this is supported by the chocolate red colour of dried blood. Presence of nitrobenzene compounds may be confirmed spectrophotometrically and estimated by the butanone test of Schrenk[1], methemoglobin levels in the blood, and urinary presence of p-nitrophenol and p-aminophenol[1,6,7].

Recommended treatment is based on the principles of decontamination and symptomatic and supportive management. Methylene blue is the antidote of choice for the acquired (toxic) methaemoglobinaemia. It is an exogenous cofactor, which greatly accelerates the NADPH-dependant methemoglobin reductase system and is indicated if the methemoglobin levels, which are more than 30%[4].It is administered intravenously at 1 – 2 mg/kg (up to 50 mg dose in adults,) as a 1% solution over five minutes; with a repeat in one hour, if necessary. Methylene blue is an oxidant at levels of more than 7 mg/kg, and therefore, may cause methaemoglobinaemia in susceptible patients. It is contraindicated in patients with G6PD deficiency, because it can lead to severe haemolysis. Ascorbic acid is an antioxidant that may also be administered in patients with methemoglobin levels of more than 30%[8]. In recent studies, N-acetylcysteine has been shown to reduce methemoglobin, but it is not yet an approved treatment for methaemoglobinaemia[8].Exchange transfusion is indicated in severe cases[4,8]. Hyperbaric oxygen is reserved only for those patients who have a methemoglobin level > 50% or those who do not respond to standard treatment.

In this case, repeated low dose methylene blue & blood transfusions helped in tiding over the fluctuating symptoms due to the release of nitrobenzene from the body stores, without exceeding the maximum dose. Fresh blood transfusion improved the oxygen carrying capacity and haemoglobin content, improving the patient symptomatically. Taking care of nutrition, adequate urine output, and hepatoprotection prevented kidney and liver failure, which have been cited as late effects.Regular use of charcoal & purgation by peglag during hospital stay may be of some help according to some centers. Forced diuresis can lead to a rapid fall in methemoglobin levels and improved discolouration. Ascorbic acid supplements are useful for follow-up management of methaemoglobinaemia.

IV. CONCLUSION

Clinitians should be aware of this uncommon,but treatable and potential serious poisoning with secondary cycling from the body tissues.

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